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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/526,348	03/16/2000	Dr. Guido Bojack	514413-3817	2532
20999	7590	01/12/2005	EXAMINER	
FROMMER LAWRENCE & HAUG 745 FIFTH AVENUE- 10TH FL. NEW YORK, NY 10151			CRANE, LAWRENCE E	
			ART UNIT	PAPER NUMBER
			1623	

DATE MAILED: 01/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/526,348

Applicant(s)

BOJACK ET AL.

Examiner

L. E. Crane

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on October 25, 2004 (amdt).
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 5-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Claims **4 and 18-21** have been cancelled, claims **1, 3 and 8** have been amended, the abstract has not been further amended, and the disclosure has not been amended as per the amendment filed October 25, 2004. No additional Information Disclosure Statements (IDSs) have been received.

Claims **1-3 and 5-17** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line **y**, the line number “y” is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claims **1-3 and 5-17** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of “undue experimentation” is appropriate are as follows.

A. The breadth of the claims is excessive in view of the number of specific embodiments listed in the Tables at pages 63-123 (11 examples) when compared with the total number of examples (a total of 698 separate examples are listed at pages 63-123).

B. The nature of the invention is compounds which are adenosine deaminase (ADA) inhibitors and their administration to mammalian hosts in need of treatment wherein ADA inhibition is necessary, or administration to plants as a herbicide, but without sufficient guidance concerning which mammalian disease conditions are to be treated and how such treatment should proceed.

C. The state of the prior art varies widely, but in some cases is very limited because the synthesis of several of the bicyclic heterocycles is presently unknown in the prior art.

D. The level of one of ordinary skill also varies widely because of the wide variation in the amount of prior art available in either the synthetic or medicinal areas depending on the ring system selected.

E. The level of predictability in the art also varies widely because of the lack of information concerning how to make or use several of the heterocyclic systems included within the scope of the claims.

F. The amount of direction provided by the inventor is quite limited because the number of examples provided (only 11 compounds characterized), wherein only a subset were tested for biological activity, and none of these tests for biological activity were conducted on whole mammalian hosts (all *in vitro* tests).

G. The existence of working examples is very limited with only 11 compounds prepared and characterized and only 5 tested for ADA activity using rabbit ADA.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure would be very substantial because of the lack of prior art teachings to guide the synthetic efforts where the bicyclic heterocycles are previously unknown and the almost complete absence of medicinal test data to guide experimentation concerning how best to effect ADA inhibition in a complete mammalian hosts. Examiner therefore concludes that, in the absence of considerably larger quantities of both synthetic and medicinal testing data, the instant claimed subject matter could only be practiced following expenditure of an undue amount of experimentation in both the synthetic and medicinal testing areas. In addition, the vast array of substituents, nested substituents, and inoperative embodiments like SF₅ (claim 1 at line 19, claim 2 at line 5, claim 4 at line 23, etc.; a very hydrolytically unstable substituent at best) make the task of the ordinary practitioner attempting to practice the instant invention even more difficult.

Applicant's arguments filed October 25, 2004 have been fully considered but they are not deemed to be persuasive.

Applicant argues that in view of *In re Marzocchi* "... 35 U.S.C. §112, [first paragraph] requires nothing more than objective enablement." Examiner would agree if claim 1 were limited as suggested elsewhere to the treatment of plants, but because the preamble of instant

claim 1 fails to specify a host, all hosts including humans are included within the scope of instant method claim 1. Therefore, the enablement standard affirmed in *Ex parte Balzarini* is deemed to continue to apply.

Applicant also argues in a conclusory manner that the amount of experimentation required is minimal without giving specific reasons in support of this conclusion. Functional claim language is still a major problem as noted below and contributes substantially to the problem of undue experimentation. In addition, both the vast number of compounds included within the scope of the numerous nested Markush groups of claim 1 and the absence of illustrative working examples for each of the numerous different heterocyclic ring systems argue against applicant's view. Applicant also argues at page 20 that "... some of the heterocyclic systems are even tautomers or stereoisomers of other heterocyclic systems." Examiner finds this comment to be technically questionable, but cannot comment further in the absence of specific examples to illustrate with complete chemical structures what applicant is talking about. And lastly, an inspection of the list of compounds in Table 1 yielded 10 examples out of more than 150 compounds wherein "physical data" was reported, meaning that the vast majority of listed compounds appear to be entirely prophetic. And in Table 2, there is no reported physical data whatsoever, suggesting that all of the examples therein are prophetic. Applicant is reminded that *Brenner v. Manson* is still good precedent and continues to stand for the proposition that a patent is granted for what is already done, and is "... not a hunting license."

Applicant may elect to address the noted deficiencies either by sharply limiting the scope of the compounds being claimed and/or by submission of additional information to establish specifically how applicant has made at least one of each and every different class of isosters of purine nucleoside compounds being claimed and/or a disclosure of specifically where in the prior art the syntheses of such compounds are reported. Or applicant may limit the method specifically to the treatment of plants.

Claims 1-3 and 5-17 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is apparently directed to a method of treating and therefore is incomplete for failure to specify either a specific disease condition being treated by said administration or -- a host in need thereof -- nb.(or preferably both).

Applicant's arguments filed October 25, 2004 have been fully considered but they are not deemed to be persuasive.

Applicant has again not responded to this grounds of rejection.

In claim 1 at lines 54-55 (formerly lines 62-64), the variable "L" is defined as "attached cyclically to the bridge G ... via a hetero atom selected from the group consisting of N, O and S," a term which incompletely describes what is being claimed because the particular structures being referred to are not provided, and because the heteroatom "N" has three valences, only two of which are provided with substituents.

Applicant's arguments filed October 25, 2004 have been fully considered but they are not deemed to be persuasive.

Applicant's response is noted but appears to not get the first point, that point being that the words provided to define variable L and its relationship to other variables do not achieve this goal. In light of the reliance of the disclosure on similarly inadequate definitions, applicant may alternatively elect to refer to the long lists of compounds in Table 1 and 2 as a basis for a generic chemical structure or structures which accurately and completely reflect the subject matter being claimed. Terms like "... may be attached cyclically to the bridge G via a second direct bond or via a hetero atom ..." are simply incompletely descriptive.

Applicant's response at p. 21, first full paragraph, suggests that applicant gets the point about the valence error in the definition of variable L, but the claim has not been amended to correct this obvious error; i.e. there is a continuing failure to specify all of the groups or atomic substituents claimed to be present at all three valences of nitrogen.

In claim 1 at lines 73-74 (previously lines 69-70), the terms "aryl" and "heterocyclyl" are incompletely defined for lack of an upper size limit or a specification of the nature and location of hetero atoms. See also the terms "substituted aryl," "heteroaryl," and "substituted heteroaryl" originally at lines 78-79 and see also dependent claims.

Applicant's arguments filed October 25, 2004 have been fully considered but they are not deemed to be persuasive.

Applicant amendment is not deemed to have been an effective response to this ground of rejection. Examiner suggests that line 87 of claim 1 should read as follows: -- where heterocyclyl is a radical derived from a saturated heterocyclic ring or an unsaturated heterocyclic ring --. Similarly in claim 1 at line 92, the line should read -- wherein heteroaryl is a radical derived from a heteroaromatic ring ... -- .

In claim 1 at lines 73-74 (originally lines 83-84 and 85), the terms "heterocyclyl" and "heteroaryl" which are generic to two classes of substituents appear to be incorrectly defined as compounds.

Applicant's arguments filed October 25, 2004 have been fully considered but they are not deemed to be persuasive.

Applicant is referred to the comments following the immediately preceding rejection.

In claim 8 at line 8, the term "Z is a precursor of the radical G-L" is incomplete because this functional description fails to describe what the structure of "Z" is. See also claims 9 and 11.

Applicant's arguments filed October 25, 2004 have been fully considered but they are not deemed to be persuasive.

Applicant refers to the disclosure, but has failed to completely describe variable "Z" in the claim. Applicant is respectfully requested to provide a complete definition of Z within the noted claim. As noted in *Regents of the University of California v. Eli Lilly* (119F.3d 1559 at 1568; 43 USPQ2d 1398 at 1406 (Fed. Cir 1997)) which MPEP §2163 at page 2100-162, column 1, quotes as follows: "A definition by function alone 'does not suffice' to describe a coding sequence 'because it is only an indication of what the gene does, rather than what it is.'" This citation is one of a number of decisions which is illustrative of the recent CAFC policy on written description which was discussed in detail at the 2000 ABA Meeting (15th Annual CLE, Intellectual Property, 4/3/2000): see also *Gentry Gallery v. Berkline*, 134 F.3d

1473, 45 USPQ 2d (Fed. Cir. 1998). For this reason, examiner respectfully disagrees with applicant's contention that "[a]pplicants .. do not believe that it is necessary to define a functional term structurally."

Claim 8 is incomplete because the term "modifying" at line 11 implies a chemical process step but fails to completely describe the process step implied. See also claim 9 at line 8 wherein the term "cyclizing" has the same problem. See also claim 11 ("condensing" and "cyclizing").

Applicant's arguments filed October 25, 2004 have been fully considered but they are not deemed to be persuasive.

Applicant asserts that "... the term 'modifying' and the like ... such as 'cyclizing,' [are] specific modification steps ... known to a person skilled in the art of chemistry and are not a specific contribution according to the invention which .. is in the structure of the final product." Examiner respectfully disagrees. The claim does not set forth any step(s) involved in the method/process, and therefore it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a process step without any active, positive steps delimiting how this use is actually practiced. And in addition, because of the lack of specific and complete structural information concerning starting material, product and reagents in the noted claim, it is presently impossible to determine which bonds are formed and/or broken during the claimed "cyclizing," "modifying," "reducing," or other step(s) being claimed herein. As to applicant assertion that the chemical structure is essentially the only contribution, the instant "claimed" chemical process steps are clearly also part of applicant's "specific contribution." And lastly, applicant appears to be using the noted terms ("cyclizing" and the like) in a manner similar to the term "utilizing" (MPEP §2173.05(q)), the noted terms therefore appear to be objectionable in view of *Ex parte Porter* (25 USPQ2d 1144 (Bd. Pat. App. Inter. 1992)).

For these reasons, examiner concludes that the metes and bounds of the claimed subject matter have not been adequately established.

Claim 5 now lacks proper antecedent basis in claim 1 because the definition of G in claim 5 has breadth in excess of that now provided for in claim 1.

Applicant's arguments with respect to claim 5 have been considered but are deemed to be moot in view of the new grounds of rejection. This rejection was necessitated by applicant's previous amendment.

Claims 7, 8, 9, 11 and 13-17 are rejected under 35 U.S.C. §112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Compound 7, 9 and 11 claims are not properly dependent from claimed directed to method of treatment claims or method of making claims and therefore each of said claims fails to limit the subject matter of the claim dependent from. Applicant is respectfully requested to incorporate all of the appropriate definitions of variables into the noted claims and to remove the incorrect dependencies from each of said claims. Additional fees for independent claims may be due to the PTO following these amendments.

In method of making claim 8, there is improper dependence from compound claim 7 and method of treatment claim 1. Examiner respectfully requests changes parallel to those suggested in the immediately preceding paragraph.

Claims 13-17 are improperly dependent because said claims are directed to the treatment of plants, a limitations not specified in claim 1. Applicant may effectively address this rejection by amendment of claim 1 to specify plants as hosts and the effects on plants expected.

Applicant's arguments with respect to claims 7, 8, 9, 11 and 13-17 have been considered but are deemed to be moot in view of the new grounds of rejection.

Claim 1 is objected to because of the following informalities:

In claim 1 at line 8, the term "is a nitrogen atom" appears twice and appears by the context to be a typographical error in the second occurrence. However, in light of the fact that the specific limitation applied to variable "E" in claim 7 do not appear in claim 1, it appears that claim 7 lacks proper antecedent basis in claim 1 unless claim 1 is amended to include the definition of E found in claim 7. See the last two lines of claim 8 for a similar problem which

examiner suggests may be made unequivocally clear by substitution of the term -- formula (I) according to claim 1 -- for the term "formula (I)."

In claim 3 at lines 9-10 and 23, the term "as defined above" is incorrect. Applicant is respectfully requested to substitute the term -- as defined in claim 1 -- wherein the indicated definitions are present.

Appropriate correction is required.

Claims 1-3 and 5-17 would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. §112.

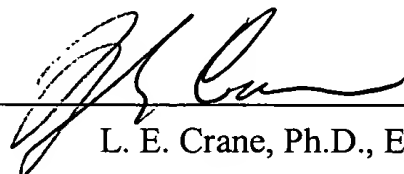
Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 703-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is 571-272-0651. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at 571-272-0661.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is 571-272-1600.

LECrane:lec
01/07/2005


L. E. Crane, Ph.D., Esq.
Patent Examiner
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